

## REMARKS

### **I. Introduction**

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claims 12-15, 22-25, 27-28, 30-31, 33-34, 36-37, 44-47, 54-57, 64-67 and 69-93 are canceled. The cancellation of claims does not constitute acquiescence in the propriety of any rejection set forth by the Examiner. Applicant(s) reserve the right to pursue the subject matter of the canceled claims in subsequent divisional applications.

Claim 1 is currently amended. Claims 6-11, 16-21, 26, 29, 32, 35, 38-43, 48-53, 58-63 and 94-95 are withdrawn.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Upon entry of this Amendment, claims 1-11, 16-21, 26, 29, 32, 35, 38-43, 48-53, 58-63, 68 and 94-95 will remain pending in the application. No new matter is added.

### **II. Response to Issues Raised by Examiner in Outstanding Office Action**

#### **a. Objection to Oath/Declaration**

The Office maintains an objection to the oath based on non-initialed or non-dated alterations. To support this contention the Office cites 37 CFR 1.52(c). This rule provides:

- (c)(1) Any interlineation, erasure, cancellation or other alteration of the application papers filed must be made before the signing of any accompanying oath or declaration pursuant to § 1.63 referring to those application papers and should be dated and initialed or signed by the applicant on the same sheet of paper. Application papers containing alterations made after the signing of an oath or declaration referring to those application papers must be supported by a supplemental oath or declaration under § 1.67. In either situation, a substitute specification (§ 1.125) is required if the application papers do not comply with paragraphs (a) and (b) of this section.
- (2) After the signing of the oath or declaration referring to the application papers, amendments may only be made in the manner provided by § 1.121.

(3) Notwithstanding the provisions of this paragraph, if an oath or declaration is a copy of the oath or declaration from a prior application, the application for which such copy is submitted may contain alterations that do not introduce matter that would have been new matter in the prior application.

Applicants note that rule 1.52 requires pages with changes to be dated and signed by the Applicant. The changes to the declaration occur in the signature block and are immediately signed and dated below the changes. As the inventor has signed and dated the page with the changes, the authenticity of the changes is not in doubt and Applicants request withdrawal of this objection.

**b. Claim Rejections - 35 U.S.C. § 112, First Paragraph**

Claims 68-69 and 93 are rejected under 35 U.S.C. § 112, second paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Office maintains, "The claimed invention is directed to an isolated or purified peptide (SEQ ID NO:3), that has at least 80% or at least 90% sequence identity to the peptide as claimed. The claims encompass a genus of variants that are highly variable. A skilled artisan cannot envision the detailed chemical structures for all the variants encompassed by the claims. Office Action, p. 4.

Applicants disagree with the Office. However, in order to further prosecution, Applicants have canceled claims 69 and 93 providing for percentage identity with the peptides of claim 1. Claim 68 is drawn to peptides with 1-5 conservative amino acid substitutions. Support for this claim is found in paragraph [0029] and original claim 68. Additionally, paragraph [0056] describes conserved amino acid substitutions involve replacing one or more amino acids of the protein of the invention with amino acids of similar size, size and/or hydrophobicity characteristics. As of the time of filing, groups of amino acids considered appropriate for substitutions had been well studied and understood by those of skill in the art. For example, William Taylor, "The Classification of Amino Acid Conservation", *J. Theor. Biol.* 119,205-218 (1986), and Bordo, et al, *J. Mol. Biol.*, 217,721-729 (1991) (See Attached), both describe the classification of amino acids well before the filing date of the application. A person of skill in the art could readily identify conservative amino acids from these applications and common knowledge at the time of filing. Based on

these disclosures, replacement of 1-5 amino acids with conservative substitutions is described in the application and a person of skill in the art would recognize that Applicants were in possession of the claimed invention at the time of filing.

Claims 68-69 and 93 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the proteins set for in SEQ ID NO: 3, does not reasonably provide enablement for any peptide having at least 80% or 90% sequence homology to SEQ ID NO: 3.

As noted above, Applicants disagree with the Office. However, in order to further prosecution, Applicants have canceled claims 69 and 93 providing for percentage identity with the peptides of claim 1. Claim 68 is drawn to peptides with 1-5 conservative amino acid substitutions.

The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom.*, *Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). See also *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). A person of skill in the art would be able to practice the claimed invention using methods described within the specification.

Although the Office maintains that substitution of conserved amino acids is not enabled by the specification, it is unclear what aspect of the experimentation is "undue experimentation" under the current case law for the standard of enablement. The currently claimed invention is to short isolated peptides and methods of utilizing these peptides. Preparation of such peptides is well known to one of skill in the art in a multitude of techniques including standard peptide synthetic technology. The Specification outlines all of the methods and tests necessary in order to use these peptides for testing activity. See the

methods outlined in the Application and used for some of the described peptides in Examples 1-14. The specification provides sufficient guidance for following the claimed methods to determine if a peptide affects the rate of degradation of type II collagen or the rate of chondrocyte hypertrophy. As noted above, as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Applicant respectfully requests reconsideration and withdrawal of the rejection.

**c. Claim Rejections - 35 U.S.C. § 102**

Claims 1, 69, and 93 are rejected under 35 U.S.C. § 102(b) as being anticipated by Qvist et al. (US Patent No. 6,110,689, August 29, 2000) and Claims 1, 68-69, and 93 over Shriners Hospitals for Crippled Children (WO 94/14070, 1994), cited on IDS filed April 30, 2004, based on the open language in the claim which reads on all of SEQ ID NO: 3 embedded in a longer sequence. Office Action, pp. 11-12 and 13-14. Applicants have canceled claims 69 and 93. Regarding claim 1, Applicants have amended the claims to recite isolated peptides consisting of the provided amino acid sequences. The claims do not encompass other peptides comprising SEQ ID NO: 3. If Applicant's explanation and amendments are not sufficient to satisfy the Office, Applicant requests clarification regarding an Amendment to specify this understanding.

In addition, there is no disclosure, teaching or suggestion in Qvist of isolated or purified peptides of SEQ ID No:3, the hydroxylated versions of this peptide with an additional glycine at the N- terminus (SEQ ID Nos: 6-9), or any of the other peptides of the present invention.

Likewise, WO 94/14070 does not teach or suggest an "isolated or purified" peptide of SEQ ID No: 3, nor the other peptides of in claim 1. Moreover, there is no teaching or suggestion in either of these references for a person of ordinary skill in the art to conclude that the peptides of the present invention would modulate and regulate cell differentiation as well as the degradation of collagen.

Applicant respectfully requests reconsideration and withdrawal of the rejection.

**CONCLUSION**

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant(s) hereby petition(s) for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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